

# United States Patent [19]

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[54] DEOXYRIBONUCLEIC ACID MOLECULES USEFUL AS PROBES FOR DETECTING ONCOGENES INCORPORATED INTO CHROMOSOMAL DNA

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[56] References Cited

## U.S. PATENT DOCUMENTS

4,490,472 12/1984 Gottlieb ..... 435/6 X  
4,535,058 8/1985 Weinberg ..... 935/78 X

## OTHER PUBLICATIONS

Taub, R. et al., Cell, 36, 339-348 (1984).  
Sheer, D. et al., Proc. Natl. Acad. Sci. USA, 80, 5007-5011 (1983).  
Tsujimoto, Y. et al., Science, 224, 1403-1406 (Jun. 29, 1984).  
Tsujimoto, Y. et al., Science, 226, 1098-1099 (Nov. 30, 1984).  
Tsujimoto, Y. et al., Nature, 315, 340-343 (May 1985).  
Tsujimoto, Y. et al., Science, 228, 1440-1443 (Jun. 21, 1985).  
Yunis, J. J., Science, 221, 227-235 (Jul. 15, 1983).  
Adams, J. M. et al., Proc. Natl. Acad. Sci. USA, 80, 1982-1986 (Apr. 1983).  
Erikson, J. et al., Proc. Natl. Acad. Sci. USA, 80, 820-824 (Feb. 1983).

Erikson, J. et al., Proc. Natl. Acad. Sci. USA, 79, 5611-5615 (Sep. 1982).

Rowley, J. D., Nature, 243, 290-292 (Jun. 1, 1973).

Rowley, J. D., Science, 216, 749-751 (May 14, 1982).

Heisterkamp, N. et al., J. Molecular and Applied Genetics, 2, 57-68 (1983).

Heisterkamp, N. et al., Nature, 299, 747-749, (Oct. 21, 1982).

de Klein, A. et al., Nature, 300, 765-767 (Dec. 1982).

de Klein, A. et al., Proc. Natl. Acad. Sci. USA, 79(24), 7824-7827 (1982).

R. Dalla-Favera et al., Science, 219 (4587), 963-967 (1983).

N. Heisterkamp et al., Nature, 306 (5940), 239-242 (1983).

Chemical Abstracts, 99:188847c (1983).

J. Groffen et al., Cell, 36(1), 93-99 (Jan. 1984).

C. M. Croce et al., Scientific American, 252(3), 54-60 (1985).

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[57] ABSTRACT

A single-stranded deoxyribonucleic acid molecule having a length of less than about 25 kb comprises at least three distinct nucleotide sequences which are the sites for incorporation into a chromosome of a deoxyribonucleic acid molecule encoding a deleterious gene. Deoxyribonucleic acid probes have been prepared from such molecules and are useful as hybridization probes for detecting chromosomal deoxyribonucleic acid which has a deoxyribonucleic acid molecule encoding a deleterious gene, i.e. oncogene, incorporated therein.

A single-stranded deoxyribonucleic acid molecule derived from human chromosome 22 which is about 5.8 kb in length contains sites for incorporation of a deoxyribonucleic acid molecule encoding the oncogene c-abl derived from human chromosome 9. Deoxyribonucleic acid probes have been prepared from this molecule and used to detect the abnormal Philadelphia chromosome and chronic myelocytic leukemia.

26 Claims, 4 Drawing Figures

